

REMARKS

Claims 11-20 and 23-32 are pending. Claims 14-15 and 26-27 were withdrawn from consideration and are canceled herein. Claims 11 and 23 have been amended to specify the site on the peptide to which the linker is attached. Applicants respectfully submit that the amendments raise no new issues, and place the application in condition for allowance, or alternatively in better condition for appeal, and therefore request entry of the amendments.

In the office action issued October 31, 2005, claims 11-13, 16-20, 23-25 and 28-32 were rejected under 35 USC § 112, second paragraph, as indefinite. Claims 11-13, 16-18, 23-25 and 28-30 were rejected under 35 USC § 103(a) as obvious over Strobel and Govindan (Bioconjugate Chemistry, hereafter "Govindan I"). Claims 11-13, 16-20, 23-25, and 28-32 were rejected under 35 USC § 103(a) as obvious over Strobel and Govindan in view of WO 99/11294 (Govindan II). The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 11-13, 16-20, 23-25 and 28-32 are rejected under 35 USC § 112, second paragraph, as indefinite. Specifically, the Examiner alleges that 11 and 23 are indefinite for failing to specify the location of the recited linker group.

Applicants have amended claims 11 and 23 to specify the location of the linker, obviating the rejection. Accordingly, applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C § 103(a)

Claims 11-13, 16-18, 23-25 and 28-30 are rejected under 35 USC § 103(a) as obvious over the combination of Strobel and Govindan (Bioconjugate Chemistry, hereafter "Govindan I"). Claims 11-13, 16-20, 23-25, and 28-32 are rejected under 35 USC § 103(a) as obvious over the combination of Strobel and Govindan in view of WO99/11294 ("Govindan"). Applicants respectfully traverse.

The Examiner states that Strobel teaches the use of a sugar-linked tyramine to radioiodinate proteins. Strobel does not, however, teach use of peptides containing D-Tyr or D-Lys. The Examiner then seeks to argue that one skilled in the art would have been motivated to modify the methods described by Strobel because of the deficiencies of the Strobel methods

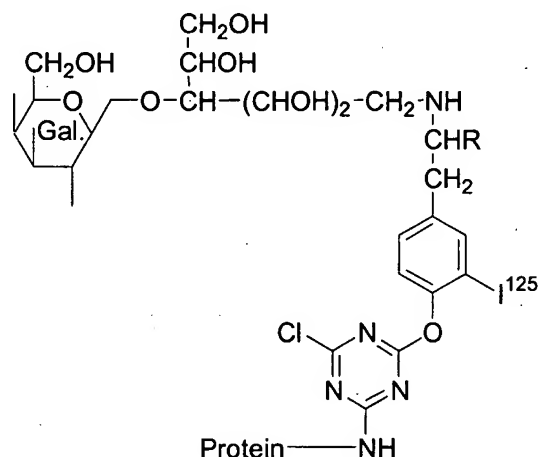
pointed out in Govindan I. Govindan I is cited as teaching a peptide comprising a D-Tyr and D-Lys that can be used for radioiodination. The Examiner's arguments fail on at least two grounds.

First, the Examiner has failed to point out why one of ordinary skill in the art would have been motivated to combine Strobel and Govindan to arrive at the instantly claimed invention. Strobel uses a carbohydrate residue, whereas the Govindan methods do not employ a carbohydrate residue. There simply is no suggestion in either reference to combine the references to arrive at applicant's instantly claimed methods. Applicants respectfully submit that the Examiner is relying on improper hindsight to find a motivation that is not present in the references. No *prima facie* case of obviousness exists and withdrawal of the rejection respectfully is requested.

Second, nothing in the combination of Govindan and Strobel would have led the skilled artisan to applicant's instantly claimed methods. The Examiner quotes Strobel as stating that the likely site of attachment of the Strobel conjugate is via the epsilon amino group of lysine residues. The relevance of this statement is not understood. This statement in Strobel clearly refers to the side chains of lysine residues on the protein to be conjugated and not to any lysine in the Strobel conjugate. Applicant's methods use peptides containing a D-lysine that is used to covalently link a reducing sugar via the lysine side chain. The peptide is then conjugated to a protein via a distinct linker moiety. This conjugation approach is quite different from that described by Strobel.

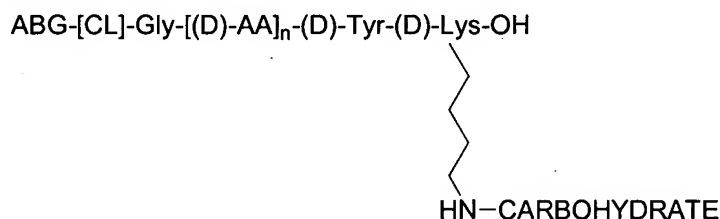
To further clarify the distinction between the methods described by Strobel and those of the present invention, applicants set forth below figures taken respectively from the Strobel paper and the present application:

Strobel:



As is clearly shown in Strobel's figure, the Strobel conjugate does not contain any lysine residues in the label portion of the conjugate. Rather, Strobel speculates that naturally occurring L-Lysine residues present on the protein moiety to which the label is attached are the likely site of attaching the glycoconjugates.

Applicant:



In contrast, applicants' conjugate specifically contains an unnatural D-Lysine residue as the C-terminus of a peptide, where the peptide can be conjugated to a protein via a distinct linker moiety [CL]. The side chain of this D-Lysine residue is employed to covalently link a reducing sugar using methods that are well known, for example, by reductive amination

Strobel therefore fails to teach or suggest the use of a peptide containing either a D-tyrosine or a D-lysine, let alone both. This deficiency is not remedied by Govindan I, which describes the use of a tyrosine containing peptide for conjugation to protein but fails to teach or suggest that the peptide should be conjugated to a carbohydrate residue, let alone that the carbohydrate should be conjugated to a D-lysine side chain. Indeed, in Govindan I the lysine side

chains are used for coupling of metal chelating residues, rather than coupling to carbohydrate. Nothing in either reference, either alone or in combination would have motivated one of ordinary skill in the art to use methods that employ a peptide having the very specific structure recited in the instant claims. Accordingly, no *prima facie* case of obviousness exists and withdrawal of the rejection respectfully is requested.

Govindan II is cited merely for the proposition that melibiose could be substituted for the dilactitol described by Strobel. However, Govindan II fails to remedy the deficiencies of the combination of Strobel and Govindan II described above, and therefore the rejection of claims 11-13, 16-20, 23-25 and 28-32 also should be withdrawn.

CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, applicants authorize the Commissioner to charge any deficiency to Deposit Account No. 08-1641.

Respectfully submitted,



Date: January 31, 2006

Heller Ehrman LLP
1717 Rhode Island Avenue, NW
Washington, D.C. 20036-3001
Telephone: (202) 912-2000
Facsimile: (202) 912-2020

Paul M. Booth, Ph.D.
Attorney for Applicants
Reg. No.: 40,244

Customer No. 26633